Post Flight Activities for the IVGEN Experiment

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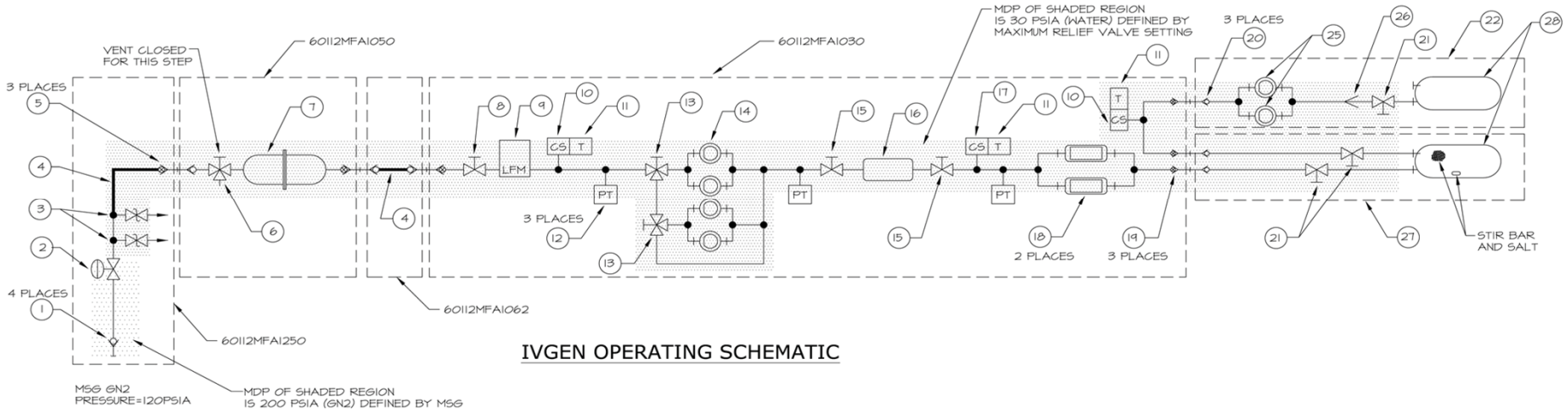
Background

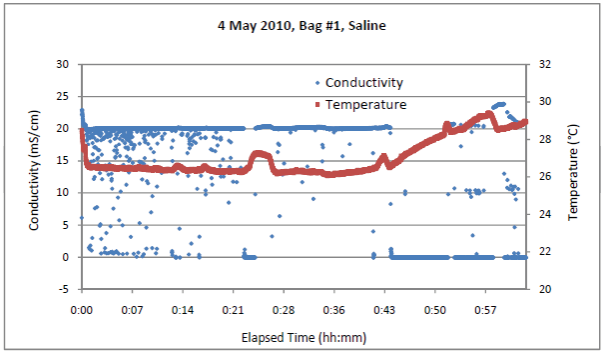
- Exploration Medical Capability (ExMC) –
  - Monitor and Treat Each Condition
  - Gap: ExMC 4.12: We do not have the capability to generate and utilize sterile intravenous fluid from potable water during exploration missions.
- Description of Hardware Function
  - Acquire & Utilize ISS Potable Water
  - Purify
  - Mix with Pharmaceutical
  - Sterilize
  - Verify Performance
    - On Orbit



IVGEN OPERATING SCHEMATIC

ISS Space Flight

- ISS Flight
  - Launch to ISS in April 2010.
  - Installed in MSG.
  - Operated 4 -6 May 2010:
    - 2 Bags of Saline Solution Produced.
    - 4 Bags of Purified Water Produced.
  - Saline Solution Returned for Evaluation per USP Standard.
  - Purified Water Recycled aboard ISS.
- ISS Results
  - Met On-Orbit Performance Requirements:
    - Flow Rate ~ 20 mlpm.
    - System Pressure Loss < 10 psid.
    - Purified Water to Conductivities less than 1 µS/cm.
    - With exception of gas bubbles, saline solution conductivities were uniform during transfer. Gas Bubbles were removed during purification process. However, mixing bags were not evacuated prior to filling and residual gas was mixed with liquid.
  - USP Testing:
    - Sterility Pass.
    - Endotoxins Pass.
    - Saline Concentrations Failed:
      - Bag 1, salt concentration too high – likely cause is not enough water.
      - Bag 2, salt concentration too low – insufficient salt premeasured into mixing bag.



Hold up Volume

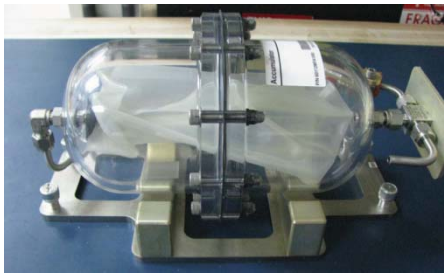
Hold-up Volume

- Dry Volume Within System Available To Be Filled With Water.
- Does Not Affect The Ability Of The System To Generate Sterile Water For Injection.
- Plays A Crucial Role In The Concentration Of The First Bag Of IV Solution as first bag is Comprised of Both Air and Water.

Source	Value (ml)
Desired	1500
Measured by USP Lab	1278
Measured mass on ISS	1266
Measured volume on ISS	1391
Post Flight Analysis	1336

Causes?

- Accumulator not full of liquid .
- Accumulator not fully vented prior to fill.
- WPA burped.
- Not all liquid was emptied from accumulator.



USP Monographs

- Sodium Chloride Injection USP 0.9%[1] (and many other injection solutions)
  - Sterility
  - Bacterial Endotoxins
  - pH
  - Heavy Metals
  - Residual Solvents
  - Various constituent assays
  - Produced with **Water for Injection**
- Water for Injection[1]
  - Bacterial Endotoxins
  - Total Organic Carbon
  - Conductivity
  - Produced from water complying with EPA National Drinking Water Regulations

Note: TOC measured in WFI, not final solution, due to complications with salts during the oxidation process

[1] Requirements listed are not all inclusive

Total organic carbon

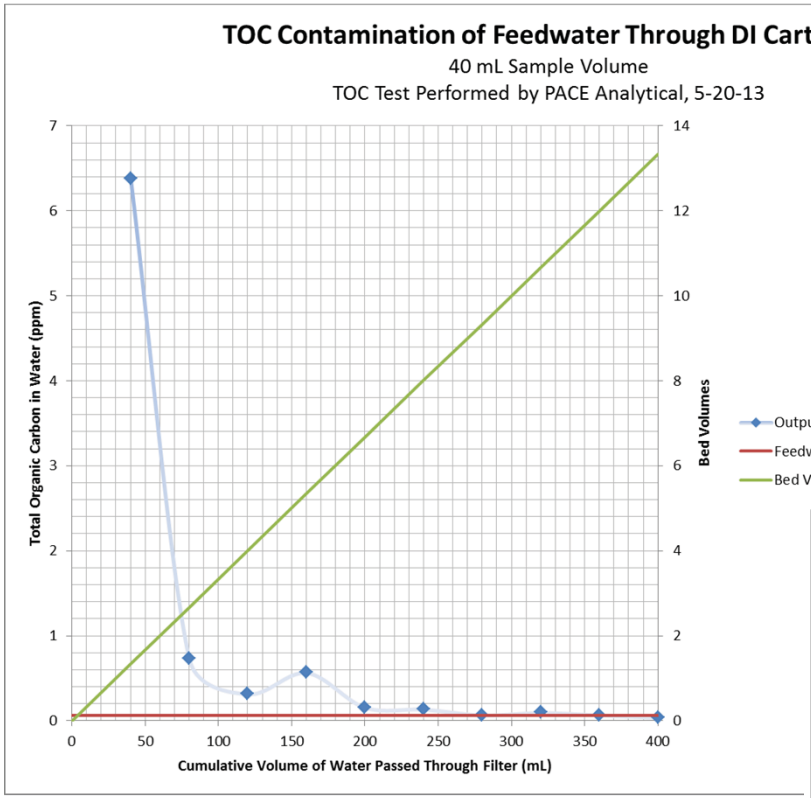
- TOC is an indirect measure of organic molecules present in pharmaceutical waters measured as carbon.
  - Total Carbon – Inorganic Carbon
  - Purge Inorganic Carbon, Measure Total Carbon
- Organic molecules are introduced into the water from
  - the source water. In water reclamation system, this would include processing waste water that may have other pharmaceuticals present.,
  - purification and distribution system materials,
  - biofilm growing in the system.
- ISS potable water supply utilizes an activated charcoal bed to remove TOC's.
- Future spacecraft water systems may not be as effective as ISS water reclamation system

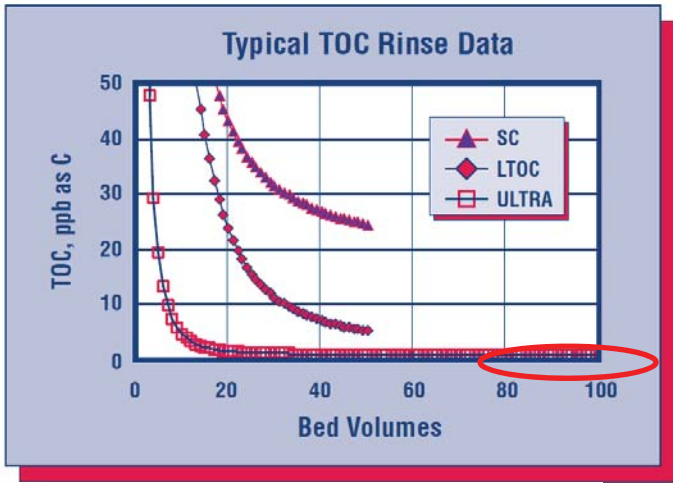
Determine Sources of contamination

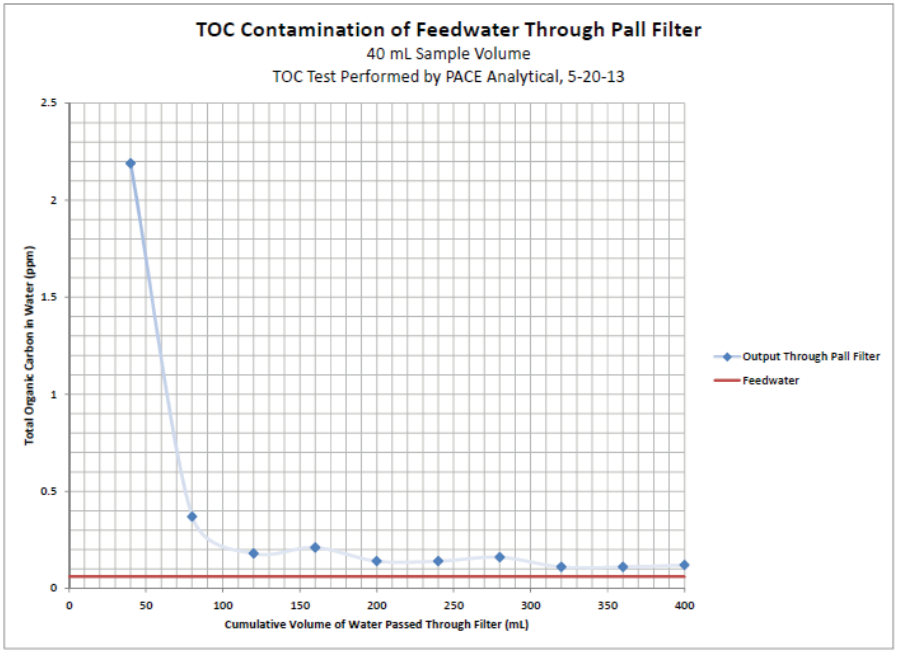
- Use High Purity Source Water
  - HPLC water
  - TOC spec of < 50 ppb
- DI Resin
- Pall membrane filters
- Tubing/Fittings
- Bag
  - Collected samples in clean glass vials

- Flow Low-TOC water through components and measure TOC level in effluent stored in glass vials
- Measurements were made in 40 ml increments as opposed to continuously.

Contamination Sources



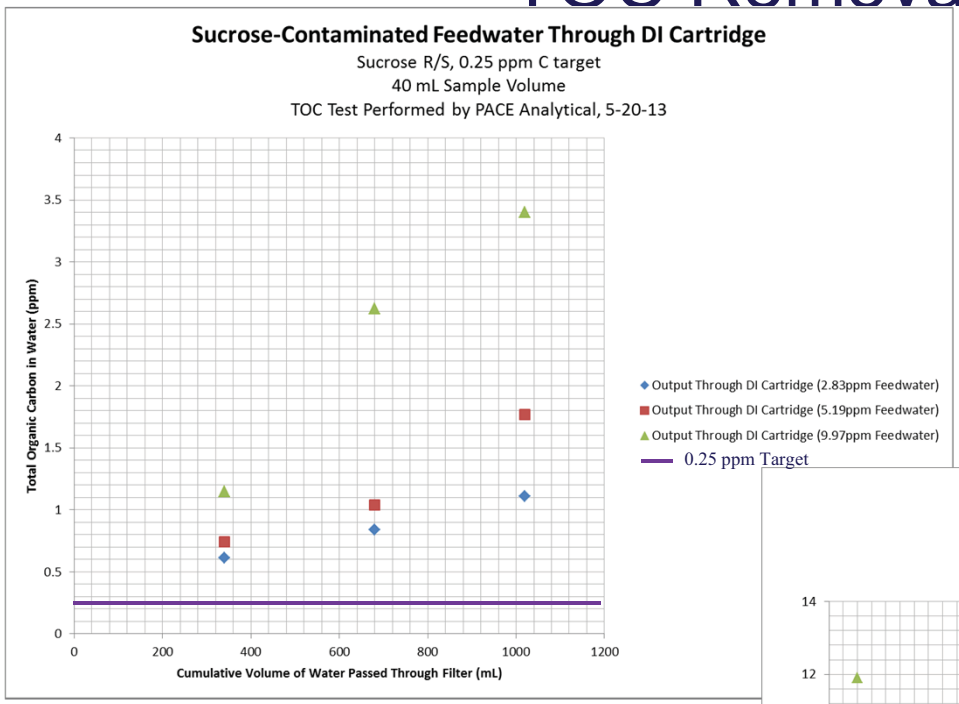


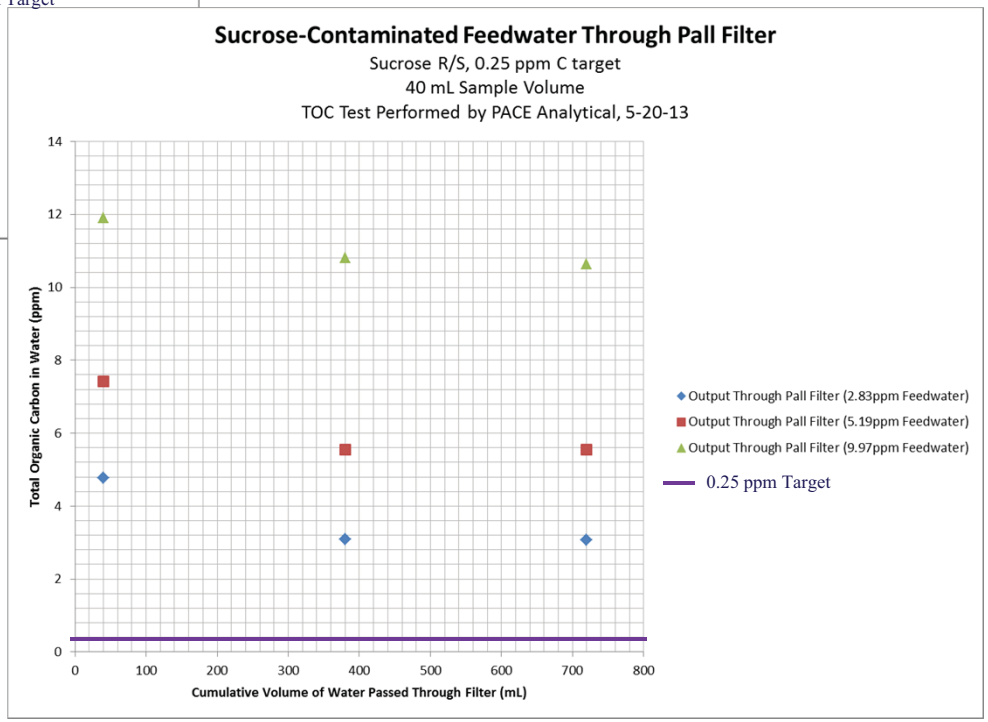


Test TOC-removal capability of filters

- Ion exchange resins can be somewhat effective at removing organics (may have polar bonding at end of organic chain)
- 0.2 micron Pall filter may be capable of removing large organic molecules.
- Flow sucrose solution through filters and measure TOC level of effluent
  - Sucrose is the reference standard used in validation of TOC removal capability
  - Vary concentrations:
    - 2.83 ppm
    - 5.19 ppm
    - 9.97 ppm

TOC Removal Capability





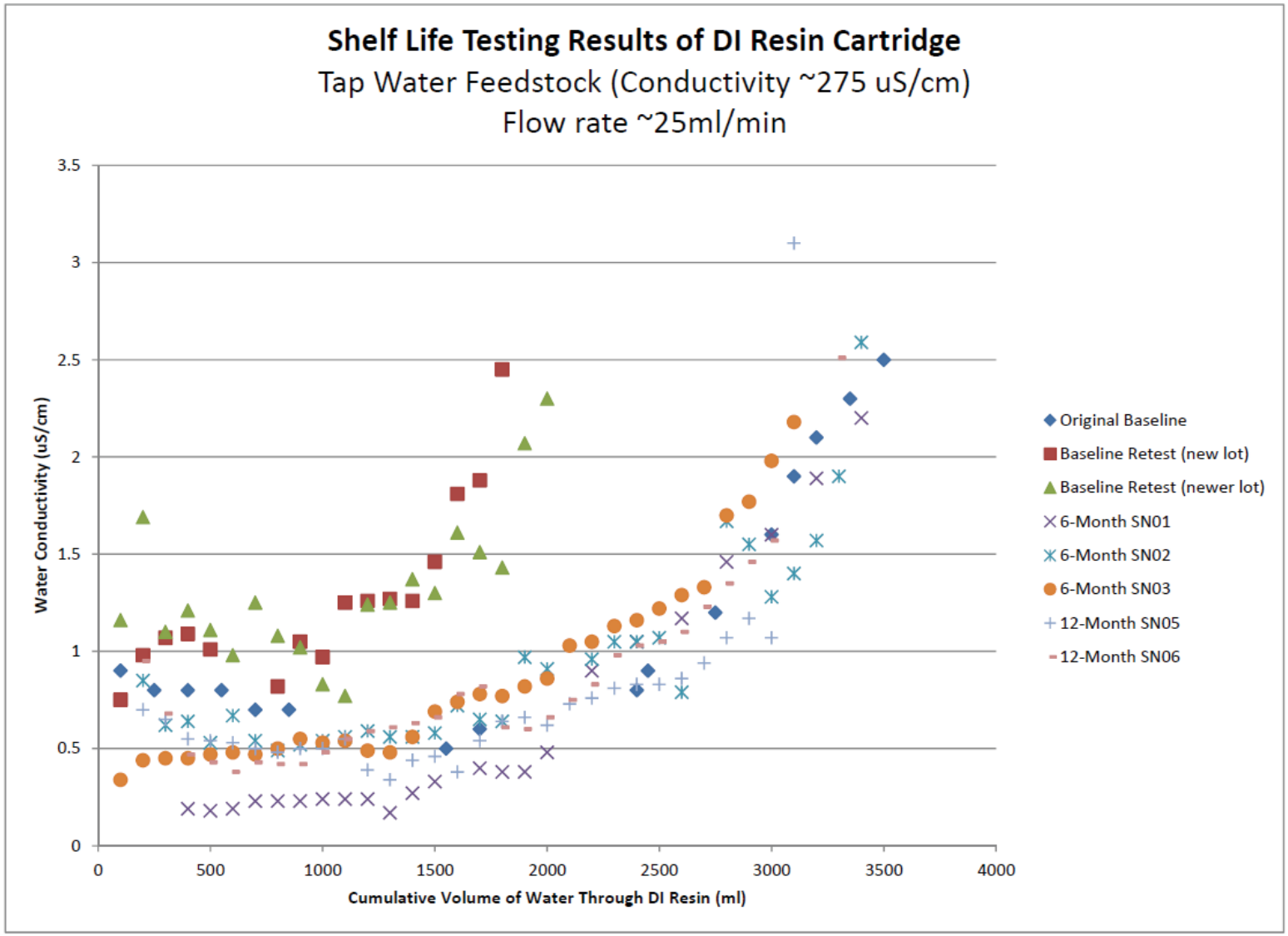
Conclusions on TOC Testing:

- TOC concentration of bulk IVGEN effluent at point of generation depends on feed water quality and bulk volume produced.
  - ISS potable water is typically TOC level below USP WFI TOC level limits (0.5ppm).
  - Bulk volumes less than 1.5L will likely exceed TOC limits due to leachables in filters (primarily ion exchange resin).
- Discarding initial product water from collected water:
  - After ~100mL for production of smaller bag (i.e. 1L), TOC's leaching from DI Resin are at acceptable levels.
  - After ~400mL of effluent production, TOCs leaching from DI Resin filter are nearly eliminated.
  - Also provides ability to purge air from system guaranteeing proper solute concentration.
  - Makes for more complicated operations

Shelf Life Testing

- Rationale:
  - DI resin performance negatively affected by humidity and exposure to air.
  - Charge on PALL filter membranes.
- Prepare Cartridges:
  - Used Fresh DI resin
  - Flight like with some minor differences.
  - Cartridge Valved off.
  - Heat Sealed in foil pouches.
  - Air physically squeezed out of pouches. No vacuum.
- Get Baseline
  - Primarily evaluation is conductivity.
  - TOC's:
  - Sterility & Endotoxins passed.
- At 6 month intervals, test a cartridge.

Conductivity Testing



Endotoxin Testing

- 6 month tests – Passed
- 12 month test – Passed

Summary

- TOC testing show that to prevent exceeding target concentrations, may need to burp at least 100 ml of water through the system prior to mixing.
  - Similar, but as severe, problem, with conductivity testing.
  - Helps to purge gas to meet targeted concentrations of pharmaceutical dissolution and mixing.
- While there is some removal of TOC's by DI cartridge, not sufficient to meet USP standards.
  - It may be necessary to incorporate an activated carbon filter if spacecraft potable water does not incorporate.
  - Several concerns that would need additional development.
- Shelf life testing is progressing.
  - Results up to 12 months are promising.
  - Each batch of DI Resin needs to be baseline tested.

Acknowledgements

- ExMC
- Pace Analytical Life Sciences, LLC
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